Fig. 1

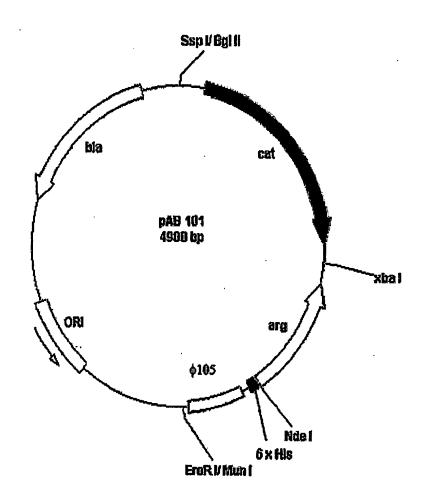


Fig. 2A

```
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181 atttaaagga tattgacata acgaaatggt tgtgtaaaac agggagatta tatcttgata
241 aggttaagaa atttgaaata gttactattc tttcccatga cgtagaaaat caaaagatta
301 taacagaatg ggagtcactc cccagagagg ctttacccga acaatttgat tcataagaac
361 taattagtag cgctttccaa tggaggcgct tttttatttg ggtagttgca taccactaaa
421 gatgttcagg tgcacatgag cattggagga aaggaacgct ttagggggaa gggaaacctt
481 taaacagtct taatccccct tgattttatg ttctctgtaa actgcgtccg gtaaatctca
541 ggatagacaa tcggcggtta acggcttgag tgcgggggca gtttagaaag aatatgattg
601 gagggattca tagatgcatc accatcacca tcatatgagc gccaagtcca gaaccatagg
661 gattattgga gctcctttct caaagggaca gccacgagga ggggtggaag aaggccctac
721 agtattgaga aaggctggtc tgcttgagaa acttaaagaa caagagtgtg atgtgaagga
781 ttatggggac ctgccctttg ctgacatccc taatgacagt ccctttcaaa ttgtgaagaa
 841 tccaaggtct gtgggaaaag caagcgagca gctggctggc aaggtggcac aagtcaagaa
 901 gaacggaaga atcagcctgg tgctgggcgg agaccacagt ttggcaattg gaagcatctc
 961 tggccatgcc agggtccacc ctgatcttgg agtcatctgg gtggatgctc acactgatat
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1261 caaggtgatg gaagaaacac tcagctatct actaggaaga aagaaaaggc caattcatct
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1381 gggaggtctg acatacagag aaggtctcta catcacagaa gaaatctaca aaacagggct
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1681 tccttctaaa gacttgttct ttcagaaaaa tgtttttcca attagtataa actctacaaa
1741 ttccctcttg gtgtaaaatt caagatgtgg aaattctaac ttttttgaaa tttaaaaagct
1801 tatattttct aacttggcaa aagacttatc cttagaaaga gaagtgtaca ttgatttcca
1861 attaaaaatt tgctggcatt aaaaataagc acacttacat aagcccccat acatagagtg
1921 ggactcttgg aatcaggaga caaagctacc acatgtggaa aggtactatg tgtccatgtc
1981 attcaaaaaa tgtgattcta ga
```

Fig. 2B

1 atgcatcaccatcaccatcat M H H H H H 22 atgagcgccaagtccagaaccatagggattattggagctcctttc M S A K S R T I G I I G A P F 67 tcaaagggacagccacgaggaggggtggaagaaggccctacagta SKGQPRGGVEEGPTV 112 ttgagaaaggctggtctgcttgagaaacttaaagaacaagagtgt LRKAGLLEKLKEQEC 157 gatgtgaaggattatggggacctgccctttgctgacatccctaat D V K D Y G D L P F A D I P N 202 gacagtccctttcaaattgtgaagaatccaaggtctgtgggaaaa D S P F Q I V K N P R S V G K 247 gcaagcgagcagctggctggcaaggtggcacaagtcaagaagaac ASEQLAGKVAQVKKN 292 ggaagaatcagcctggtgctgggcggagaccacagtttggcaatt G R I S L V L G G D H S L A I 337 ggaagcatctctggccatgccagggtccaccctgatcttggagtc GSISGHARVHPDLGV 382 atctgggtggatgctcacactgatatcaacactccactgacaacc IWVDAHTDINTPLTT 427 acaagtggaaacttgcatggacaacctgtatctttcctcctgaag T S G N L H G Q P V S F L L K 472 gaactaaaaggaaagattcccgatgtgccaggattctcctgggtg E L K G K I P D V P G F S W V 517 actccctgtatatctgccaaggatattgtgtatattggcttgaga T P C I S A K D I V Y I G L R 562 gacgtggaccctggggaacactacattttgaaaactctaggcatt D V D P G E H Y I L K T L G I 607 aaatacttttcaatgactgaagtggacagactaggaattggcaag K Y F S M T E V D R L G I G K V M E E T L S Y L L G R K K R 697 ccaattcatctaagttttgatgttgacggactggacccatctttc PIHLSFDVDGLDPSF 742 acaccagctactggcacaccagtcgtgggaggtctgacatacaga T P A T G T P V V G G L T Y R 787 gaaggtetetacateacagaagaaatetacaaaacagggetacte EGLYITEEIYKTGLL 832 tcaggattagatataatggaagtgaacccatccctggggaagaca S G L D I M E V N P S L G K T 877 ccagaagaagtaactcgaacagtgaacacagcagttgcaataacc PEEVTRTVNTAVAIT 922 ttggcttgtttcggacttgctcgggagggtaatcacaagcctatt L A C F G L A R E G N H K P I 967 gactaccttaacccacctaagtaa 990 DYLNPPK*

Fig. 2C

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Fig. 3

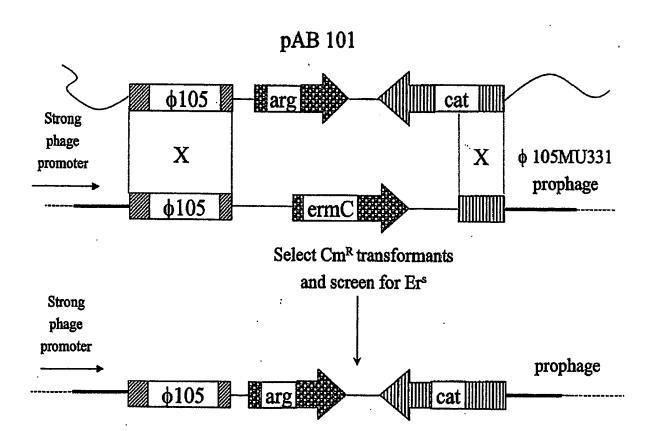
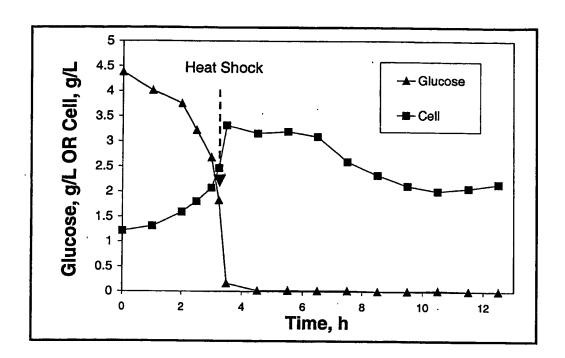


Fig. 4A



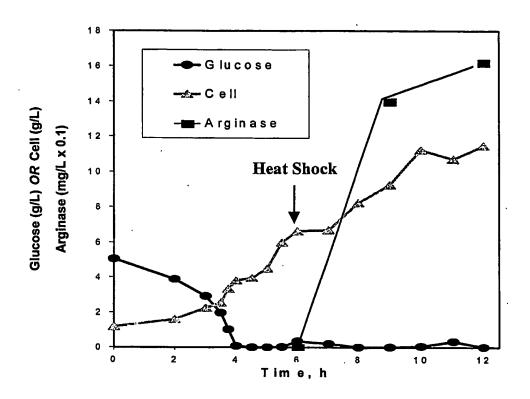


Fig. 4B



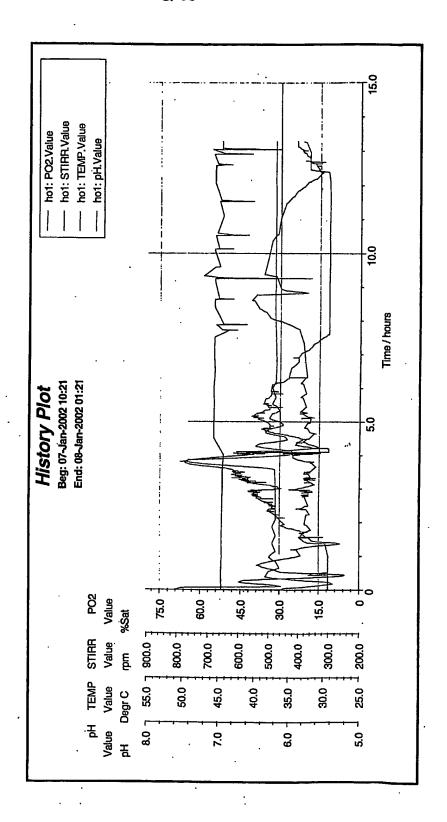
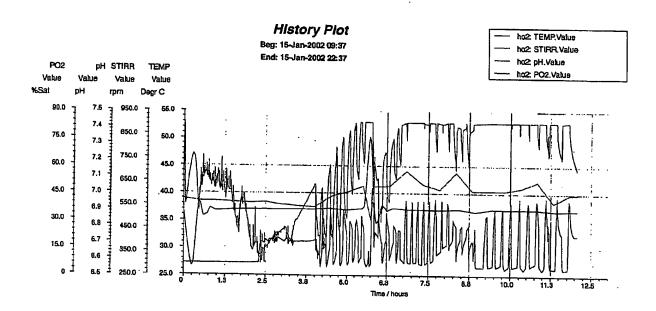


Fig. 5B



15.0

Waste

min

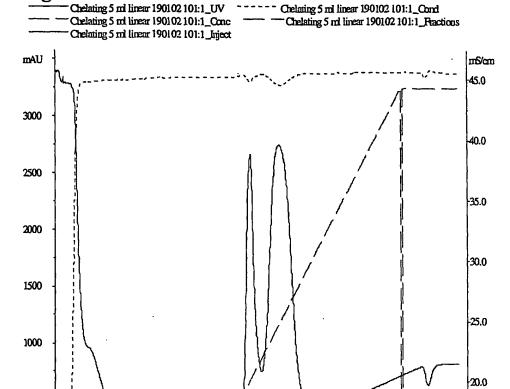
10/46



500

0

0.0

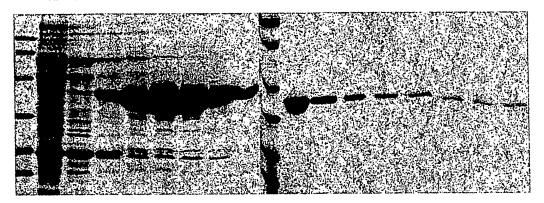


HiTrap_Chelating_1x5_ml 0.8 (MPa) 5.00 (ml/min) Column Pressure_limit Flow UV_Averaging_time 2.60 0.00 {%B} Start_ConcB Equilibrate_with 0.5 (CV) Flowthrough_FracSize 8 Empty_loop_with
Wash_column_with
Start_Frac_at {ml} (CV) {%B} Eluate_FracSize (ml) End_Frac_at 100 (%B) Target_ConcB_1 100` (%B) Length_of_gradient_1 10 (base) 0 {%B} Target_ConcB_2 Length_of_gradient_2 0 Target_ConcB_3 {%B} Length_of_gradient_3 0.00 (base) 100 (%B) (CV) Conc_of_eluent_B Clean_with 0.00 {%B} 0.00 (CV) Reequilibrate_conc Reequilibrate_with

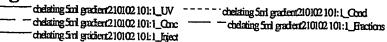
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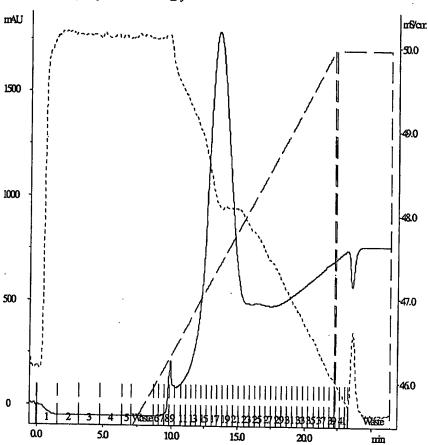
Fig. 6B

M 11 12 13 14 15 16 17 18 M 19 20 21 23 25 27 29 31









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Eluate_FracSize 10 {%B} (ml) End_Frac_at 100 {%B} Target_ConcB_1 100 (%B) Length_of_gradient_1 15 {base} Target_ConcB_2
Length_of_gradient_2
Target_ConcB_3 0 {%B} 0.00 {base} {%B} 0.00 {base} 100 {%B} Length_of_gradient_3 Conc_of_eluent_B 4.00 (CV) 0.00 (%B) Clean_with Reequilibrate_conc Reequilibrate_with 0.00 (CV)

PCT/GB2003/002665

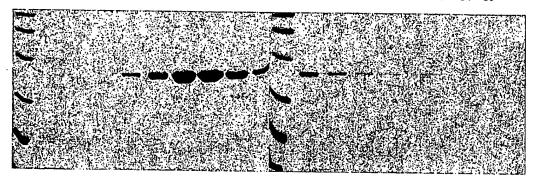
WO 2004/000349

13/46

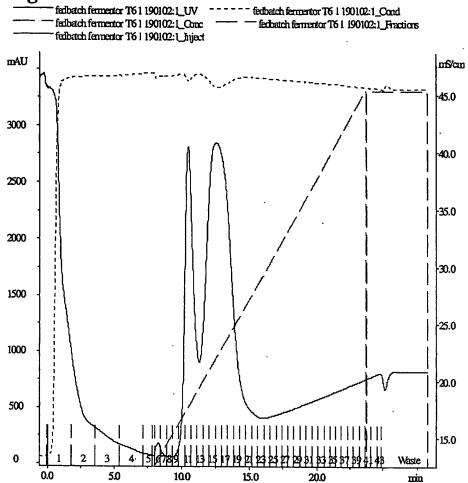
10/518223

Fig. 7B

 $\ \, M \quad 9 \quad 10 \quad 11 \quad 13 \quad 15 \quad 17 \quad 19 \quad 21 \quad 23 \quad M \quad 25 \quad 27 \quad 29 \quad 31 \quad 33 \quad 35 \quad 37 \quad 39$



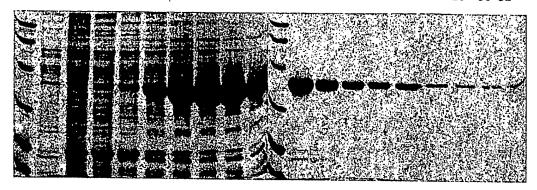




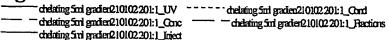
Column HiTrap_Chelating_1x5_ml 0.8 (MPa) 5.00 (ml/min) Pressure_limit Flow UV_Averaging_time Start_ConcB 2.60 0.00 {%B} Equilibrate_with 0.5 (CV) Flowthrough_FracSize 8 (ml) Empty_loop_with (ml) Wash_column_with Start_Frac_at Eluate_FracSize (ĆV) {%B} (ml) End_Frac_at {%B} Target_ConcB_1 100 {%B} Length_of_gradient_1
Target_ConcB_2
Length_of_gradient_2
Target_ConcB_3 14 (base) 0 0 {%B} 0.00 {base} 0 {%B} Length_of_gradient_3 0.00 {base} Conc_of_eluent_B 100 (%B) 4.00 {CV} : 0.00 {%B} 0.00 {CV} Clean_with Reequilibrate_conc Reequilibrate_with

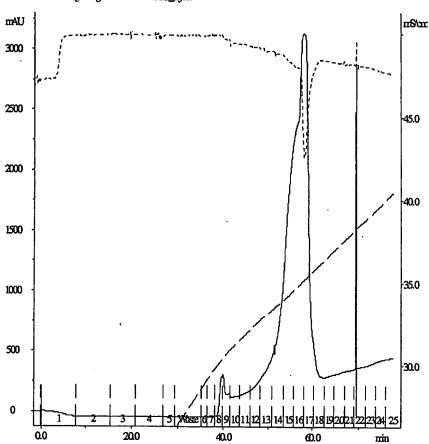
Fig. 8B

M 10 11 12 13 14 15 16 17 18 M 19 20 21 22 24 26 28 30 32









Column HiTrap_Chelating_1x5_ml 0.8 {MPa} 5.00 {ml/min} Pressure_limit Flow UV_Averaging_time 2.60 Start_ConcB 0.00 {%B} Equilibrate_with 0.2 (CV) Flowthrough_FracSize 8 {r {ml} Empty_loop_with 0 {ml} Wash_column_with Start_Frac_at {%B} Eluate_FracSize End_Frac_at (ml) 100 {%B} Target_ConcB_1 100 {%B} Length_of_gradient_1 15 Target_ConcB_2 {%B} Target_ConcB_2 (%B)
Length_of_gradient_2 0.00 {base}
Target_ConcB_3 0 {%B}
Length_of_gradient_3 0.00 {base}
Conc_of_eluent_B 100 {%B} 4.00 (CV) Clean_with 0.00 (%B) 0.00 (CV) Reequilibrate_conc Reequilibrate_with

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Fig. 9B

M 8 10 12 14 15 16 17 18 19 M 20 22 24 E1 E2 E3 E4 E5 E6

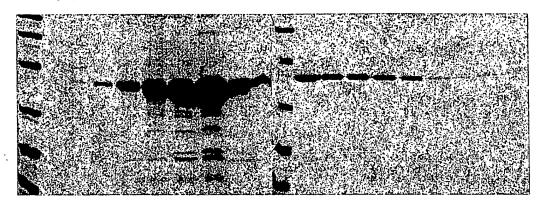


Fig. 10

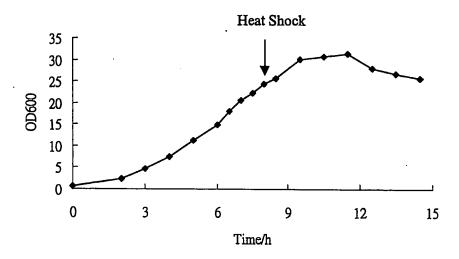


Fig. 11

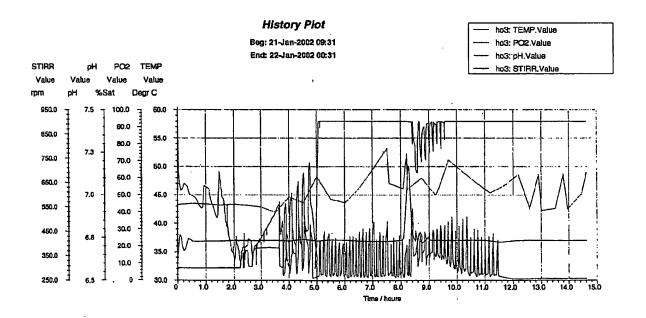
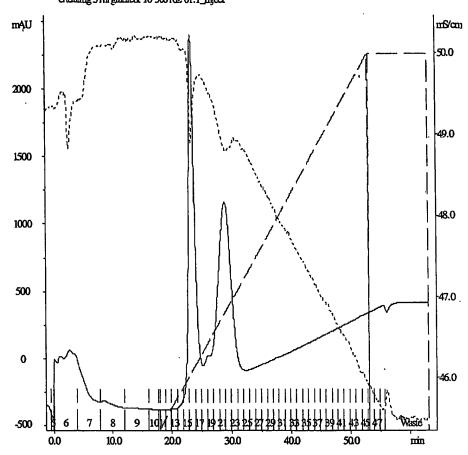


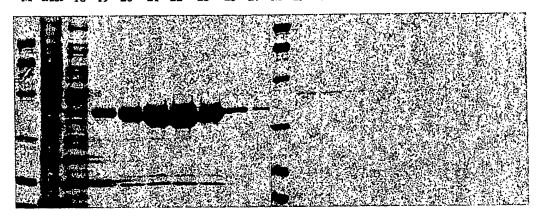
Fig. 12A



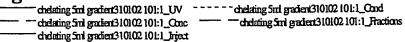
HiTrap_Chelating_1x5_ml Column Pressure_limit 0.5 {MPa} Flow {ml/min} UV_Averaging_time Start_ConcB 2.60 0.00 {%B} Equilibrate_with {ČV} Flowthrough_FracSize Empty_loop_with {ml} Wash_column_with {ĆV} Start_Frac_at {%B} Eluate_FracSize (ml) End_Frac_at 100 {%B} Target_ConcB_1 14 {base} Length_of_gradient_1 0 (%B) 0.00 (base) Target_ConcB_2 (Length_of_gradient_2 {%B} Target_ConcB_3 0.00 {base} Length_of_gradient_3 Conc_of_eluent_B 100 {%B} 4.00 {CV} : 0.00 {%B} 0.00 {CV} Clean_with Reequilibrate_conc
Reequilibrate_with

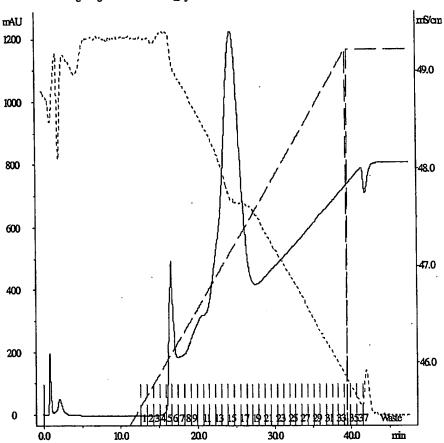
Fig. 12B

M crude 16 19 20 21 22 23 25 27 M 29 31 33 35 37 39 41 43 45









HiTrap_Chelating_1x5_ml 0.8 {MPa} 2.5 {ml/min} Column Pressure_limit Flow UV_Averaging_time Start_ConcB 2.60 0.00 {%B} Equilibrate_with 0 {CV} Flowthrough_FracSize 0 {r (ml) 6.5 (CV) Empty_loop_with 0 Wash_column_with Start_Frac_at
Eluate_FracSize 5 {%B} 2 (ml) End_Frac_at 100 (%B) {%B} Target_ConcB_1 100 Length_of_gradient_1 (base) Target_ConcB_2 Length_of_gradient_2 Target_ConcB_3 0 (%B) 0.00 (base) 0.00 (base) 0.00 (base) 100 (%B) Length_of_gradient_3 Conc_of_eluent_B 4.00 (CV) Clean_with 0.00 (%B) 0.00 (CV) Reequilibrate_conc Reequilibrate_with

Fig. 13B

M 7 9 11 12 13 14 15 16 17 M 18 20 22 24 26 28 30 32 34

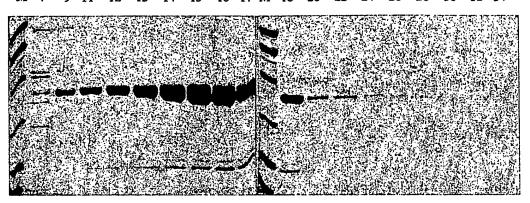
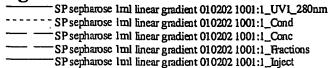
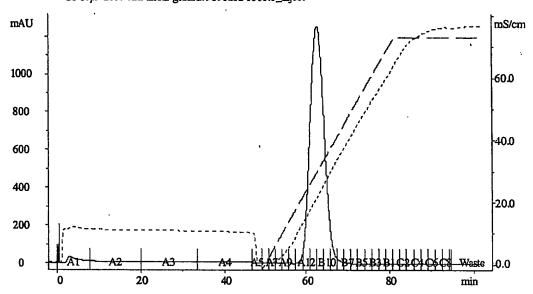


Fig. 14A





Column HITrap_SP_FF_1_ml Flow_Rate 1.00 {ml/mln} Column_PressureLimit 0.40 {MPa} Wavelength_1 280 (nm) Wavelength_2 OFF (nm) {nm} Wavelength_3 OFF 5.12 {sec} Averaging_Time_UV Pump_A_Inlet Pump_B_Inlet В1 Wash_Inlet_A1_ OFF Wash_Inlet_A2_ OFF Wash_Inlet_B1_ Wash_Inlet_B2_ OFF OFF Start_ConcB Compensation_Volume 8 (CV) Equilibrate_with Flowthrough_TubeType 18mm
Flowthrough_FracSize 8 (ml)
Flowthrough_StartAt FirstTube Empty_loop_with 31.500 (ml) Wash_column_with _Start_Frac_at {%B} _End_Frac_at 100 {%B} TubeType_EluateFrac 18mm Eluate_Frac_Size (ml) NextTube EluateFrac_StartAt Target_ConcB 100 {%B} Length_of_Gradient 20.00 (base) 8 (ml) (CV) Gradient_Delay 5.00 Clean_with

Fig. 14B

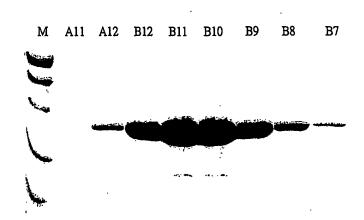
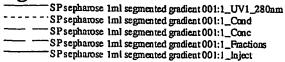
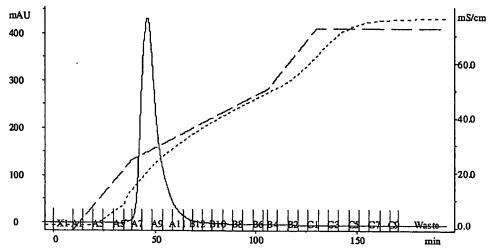


Fig. 15A





Column HITrap_SP_FF_1_ml Flow_Rate 0.40 {ml/min} Column_PressureLimit 0.50 {MPa} 280 (nm) OFF (nm) Wavelength_1 (nm) (nm) Wavelength_2 Wavelength_3 OFF Averaging_Time_UV 5.12 (sec) Pump_A_Inlet Pump_B_Inlet Wash_Inlet_A1 Wash_Inlet_A2_ Wash_Inlet_B1_ **OFF** Wash_inlet_B2_ OFF Start_ConcB {%B} Compensation_Volume 8 Equilibrate_with Flowthrough_TubeType 30mm Flowthrough_FracSize 40 {ml} Flowthrough_StartAt TubeNumber[X.1] Empty_loop_with 0.000 (ml) Wash_column_with 2 (CV) 1_Tube_Type 18mm 1_Fraction_Size {ml} FirstTube 1_Start_at Target_ConcB_1 35 {%B} 6.00 {base} Length_of_Gradient_1 2_Tube_Type 18mm 2_Fraction_Size (ml) NextTube 2_Start_at Target_ConcB_2 70 (%B) Length_of_Gradient_2 14.00 (base) 3_Tube_Type 18mm 3_Fraction_Size (ml) NextTube 3_Start_at Target_ConcB_3 100 (%B) 5.00 (base) Length_of_Gradient_3 Gradient_Delay (ml) Clean_with 5.00 (CV)

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Fig. 15B

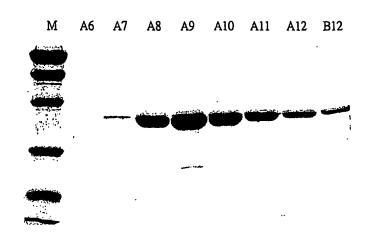


Fig. 16A

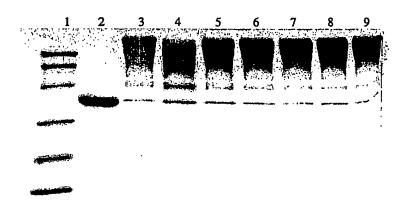


Fig. 16B

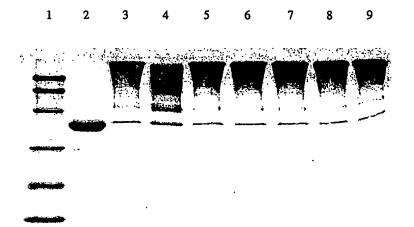
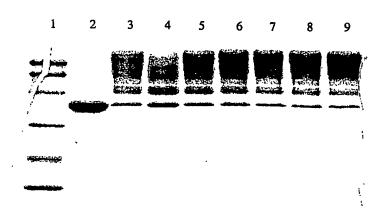


Fig. 17A



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Fig. 17B

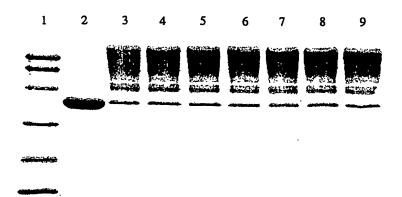


Fig. 18A

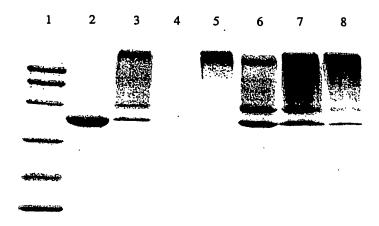
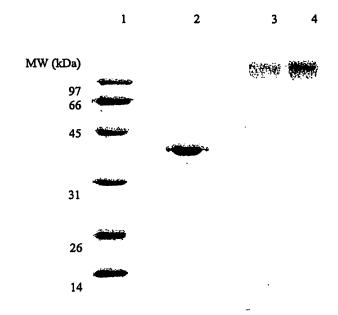


Fig. 18B



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Fig. 19A

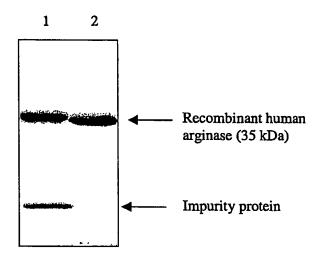
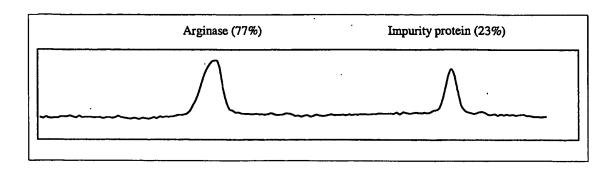


Fig. 19B



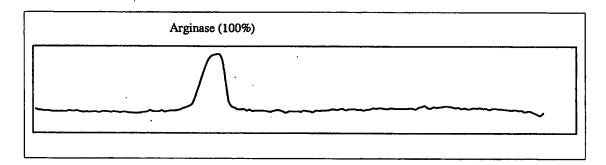


Fig. 20

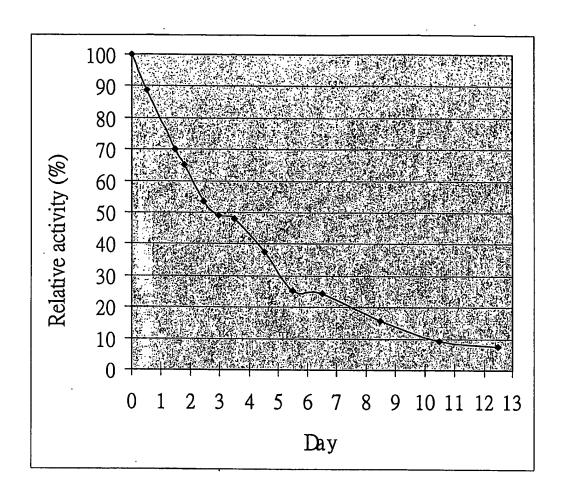
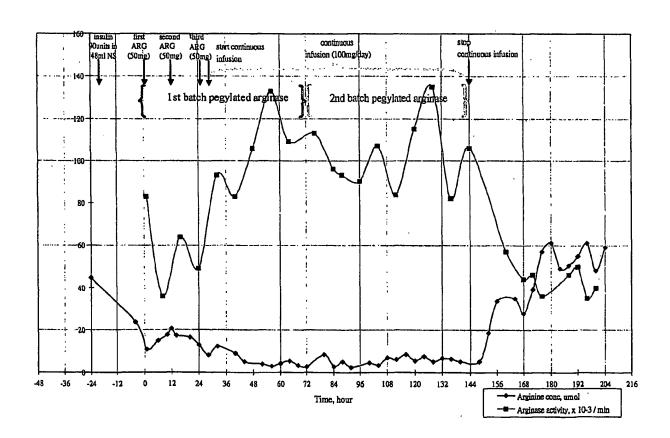
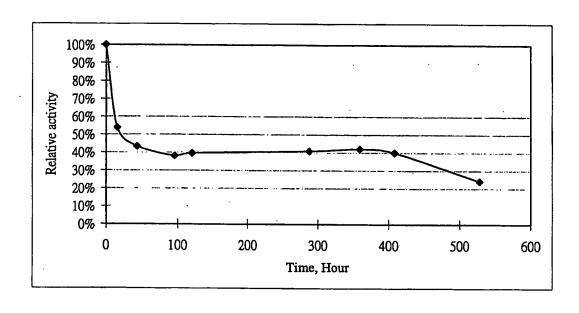


Fig. 21



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Fig. 22



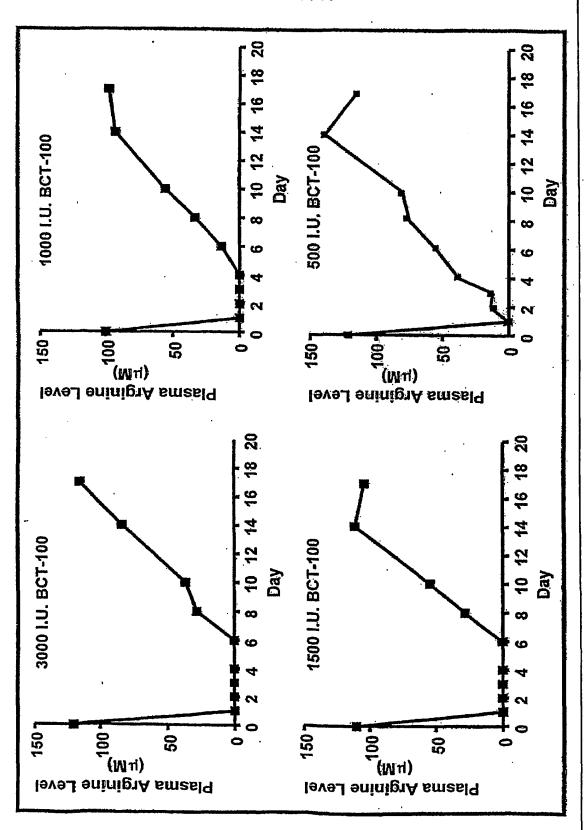
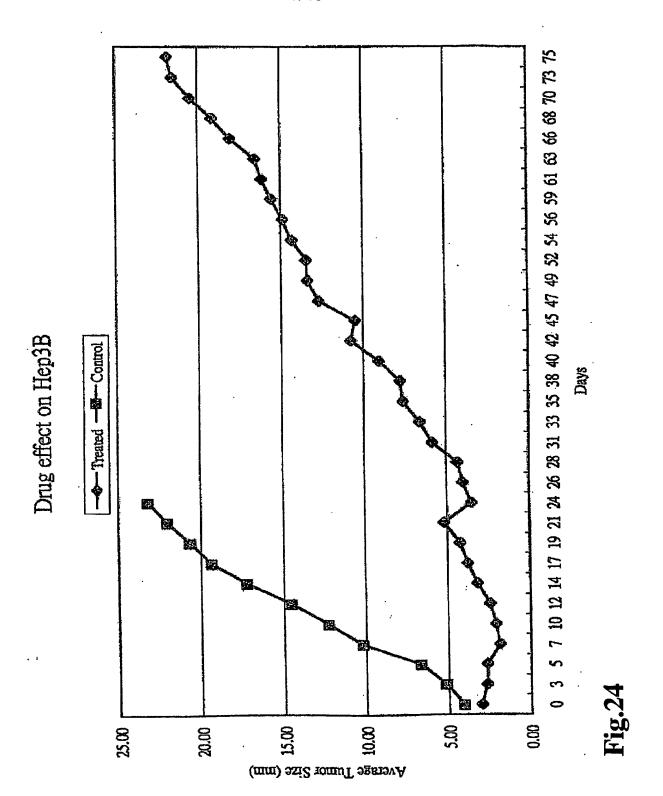


Fig. 23



Drug effect on PLC/PRF/5 -Size changes

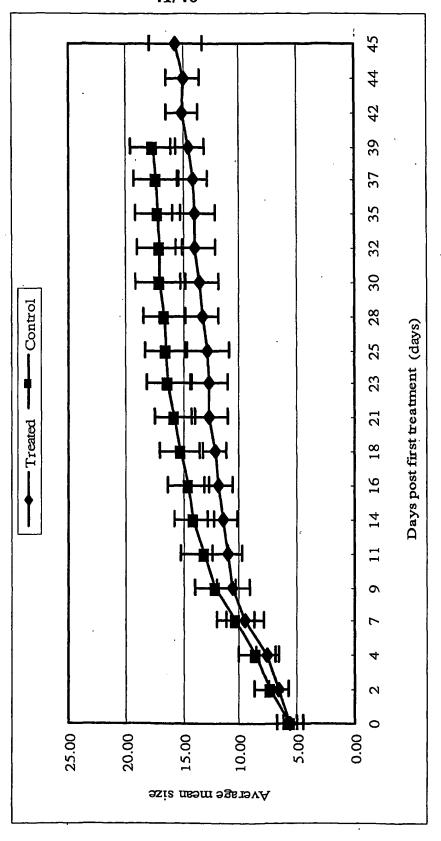


Fig. 25A

Drug effect on PLC/PRF/5 -Weight changes

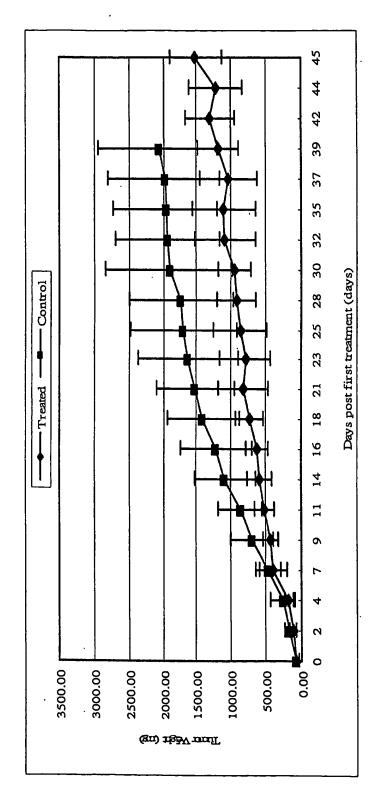


Fig. 25

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Drug effect on Huh-7 – Weight changes

Drug effect on Huh-7 - Size changes

Fig. 26B

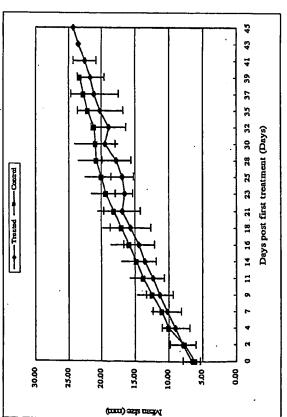


Fig. 26A

Drug effect on MCF-7 – Size changes

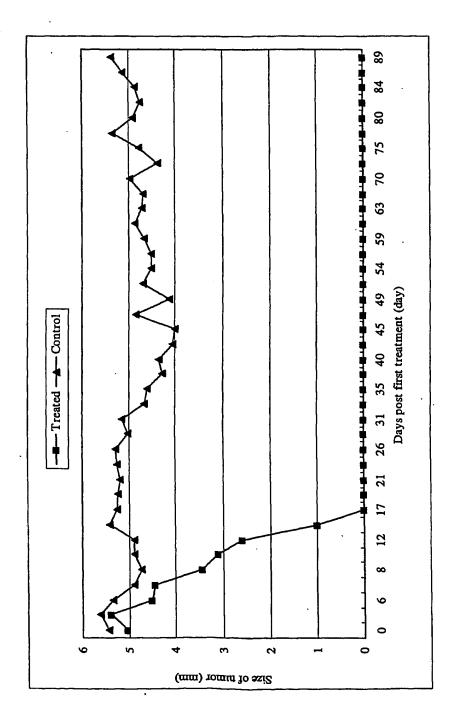
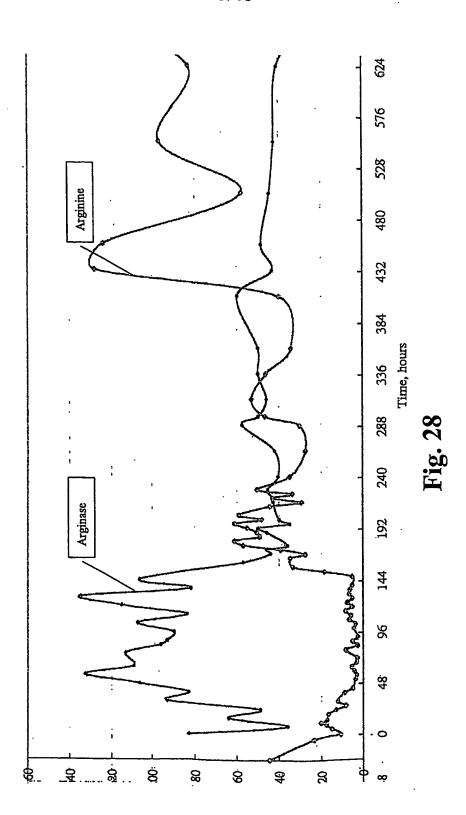
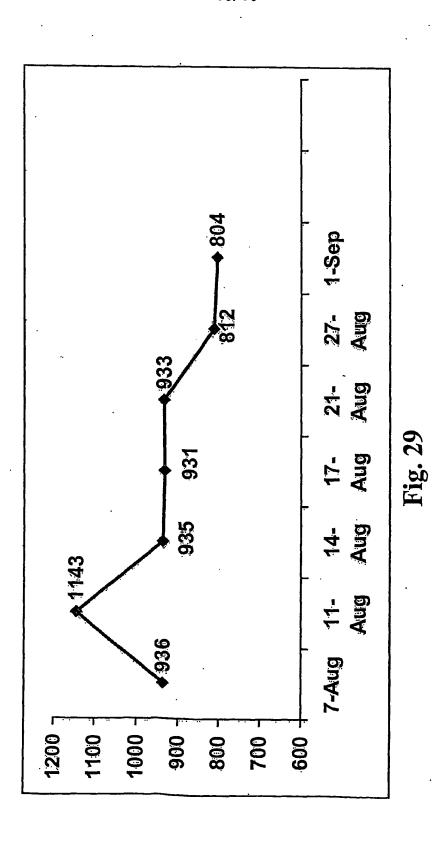


Fig. 27

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